

- (19) Japan Patent Office (JP)
- (12) Laid-Open Patent Gazette (A)
- (11) Japanese Laid-Open Patent Application No. HEI 9-206026
- (43) Published On: August 12, 1997

(51)	Int. Cl ⁷	Classification Codes	Patent Office Control Nos.	F1	Technical Indicators
	A23L 1/30		A23L 1/30		B
	A23G 1/00		A23G 1/00		
	A23L 1/221		A23L 1/221		C
//	A61K 35/78		A61K 35/78		AAEC
	Request for examination: None				
	Number of claims: 4				
	Total pages in original: 5				

(21) Filing No: HEI 8-22848

(22) Filing Date: February 8, 1996

(71) Applicant: 000006091

Meiji Seika Kaisha, Ltd.

4-16 2-chome, Kyobashi, Chuo-ku, Tokyo

(72) Inventor: Yoshio Yamaki

Meiji Seika Kaisha, Ltd. Biological Science Laboratory

5-3-1 Chiyoda, Sakato, Saitama

(72) Inventor: Uyako Ito

Meiji Seika Kaisha, Ltd. Biological Science Laboratory

5-3-1 Chiyoda, Sakato, Saitama

(72) Inventor: Akihiro Kodaira

Meiji Seika Kaisha, Ltd. Biological Science Laboratory

5-3-1 Chiyoda, Sakato, Saitama

(72) Inventor: Choshio Takizawa

Meiji Seika Kaisha, Ltd. Biological Science Laboratory

5-3-1 Chiyoda, Sakato, Saitama

(72) Inventor: Takashi Adachi

Meiji Seika Kaisha, Ltd. Biological Science Laboratory

5-3-1 Chiyoda, Sakato, Saitama

(54) Title of the Invention:

Food or Drink Item Promoting Stress Prevention and Adaptive Development

(57) Summary

[OBJECT] To counter stress by offering a food or drink item which prevents stress or promotes adaptive development safely and without suppressing the central nervous system.

[MEANS FOR SOLUTION] A cacao bean-derived extract was obtained and the content of said extract was discovered to have superior effects including prevention of a stress-induced decrease in emotional and behavioral response and promotion of adaptive development. The addition of said extract affords a food or drink item which is safe and does not suppress the central nervous system and which has the effects of preventing stress and promoting adaptive development simply, easily, and at a low cost.

[CLAIMS]

[FIRST CLAIM] A food or drink item which contains a cacao bean-derived extract.

[SECOND CLAIM] The food or drink item pertaining to Claim 1, wherein said extract is extracted from a cacao bean using ethanol

[THIRD CLAIM] The food or drink item pertaining to Claim 1, which, due to the inclusion of a cacao bean-derived extract, exhibits an effect of preventing a stress-induced decrease in emotional and behavioral response.

[FOURTH CLAIM] The food or drink item pertaining to Claim 1, which, due to the inclusion of a cacao bean-derived extract, exhibits an effect of promoting adaptive development to stress.

[0001]

[FIELD OF THE INVENTION] The present invention concerns a food or drink item containing a cacao bean-derived extract. In further detail, the present invention concerns a food or drink item which prevents a decrease in emotional and behavioral response otherwise caused by psychological or physiological stress. In further detail, the present invention concerns a food or drink item which promotes adaptive development to stress.

[0002]

[DESCRIPTION OF THE RELATED ART] The cacao (*Theobroma cacao*) is a low elevation evergreen tree of the *Sterculia* family native to moist regions of the tropical Americas and produces a fruit 15 to 30cm in length and 10cm in diameter. The cacao tree has reportedly been cultivated and domesticated for over 2000 years, and its fruit the cacao bean is used as an ingredient in chocolate, cocoa, and other food and drink items. The cacao bean has also been reported to have physiologic effects including a cardiogenic effect and a diuretic effect, but an effect against stress has not been reported.

[0003] There are various forms of stress such as those induced by daily temperature changes, human relationships, and life in complex modern society, and the response to these stresses affects physical and mental well-being. Illnesses induced by physical or mental stress are also proliferating rapidly in modern, information-overloaded society (Siltanen, P., Clin.

Res., 16, 142-155, 1984). In response thereto, research concerning acute or repetitive stress is also being pursued actively in the fields of neurology and neuropharmacology (Bliss, E. L. and Ailion, J., Life Sci., 10, 1161-1169, 1971).

[0004] A highly repetitive burden of a consistent stress is known to weaken stress responses gradually (Kennett, G. A., Dickinson, S. L. and Curzon, G., Brain Res., 330, 253-263, 1985). This decline in responsiveness in the form of acclimatization to stress or a phenomenon termed adaptive development is regarded as one important biodefense mechanism (Kennett, G. A., Dickinson, S., L. and Curzon, G., Eur. J. Pharmacol., 119, 143-152, 1985).

[0005] Benzodiazepine-based antianxiety drugs have heretofore been the main vehicle used to alleviate stress and prevent illness. By suppressing the central nervous system, these drugs temporarily block external stimuli and provide recovery. These drugs are highly safe but have the potential to be somewhat habit-forming in continued usage and to cause side effects.

[0006]

[PROBLEMS THE INVENTION INTENDS TO SOLVE] When antianxiety drugs are used to suppress the higher central nervous system and counter such stress, appropriate decisions and responses can no longer be made, and the adaptation which originally served as a defense mechanism is ultimately impaired. Development of a food or drink item which is safe and does

not suppress the central nervous system has been sought as a means of stress prevention or recovery or to promote adaptive development.

[0007]

[MEANS USED TO SOLVE THE AFOREMENTIONED PROBLEMS] After repeated and painstaking research intended to solve the aforementioned problems, the present inventors completed the present invention on the basis of knowledge embodied in their novel discovery that an extract derived from the cacao bean has a stress-preventing effect and also has a superior effect of promoting adaptive development and does not suppress the central nervous system.

[0008]

[PREFERRED EMBODIMENT OF THE INVENTION] A method for manufacturing a cacao bean-derived extract pertaining to the present invention is extraction from the cacao bean using ethanol. The cacao bean as an ingredient is used in various forms including cacao shell, cacao nib, cacao mass, and defatted cacao mass, but defatted cacao mass is preferable in that it allows an extract to be made a powder. Defatted cacao mass is obtained by removing the fat component from cacao mass stripped of a husk termed a cacao shell. The oil component may be removed acceptably by a well-known method.

[0009] In the extraction method, 300-800 wt parts and preferably 400-700 wt parts ethanol solution is added to 100 wt parts cacao bean, and mixing is carried out at ambient temperature for several hours to 48 hours and preferably for approximately 24 hours. The ethanol solution used may be one with a water to ethanol ratio from 60:40 to 0:100 and preferably from 30:70 to 0:100. Ethanol contained in a liquid extract obtained by filtering is removed under reduced pressure, and a liquid extract is obtained. The liquid extract can also be made a powder by freeze-drying or reduced pressure drying, etc. An extract thus obtained can be used as either a liquid concentrate or a powder as required by a food item application. According to the food item application, the extract can of course also be further refined by chromatography or the like.

[0010] When stress is encountered, the body manifests various reactions. In gross distinction these include behavioral responses (such as quantitative changes in food or liquid intake, as well as quantitative changes in voluntary activity after removal of the stress burden), emotional responses (such as changes in emotions including investigative behavior, evasive behavior, crying, or bowel movements), and physiological responses (including changes in body weight or temperature, as well as changes in the digestive, circulatory, and endocrine systems).

Assessment of adaptive development, deemed one important defense mechanism of the body against stress, is widely used as an index of such stress responses induced by a psychological or physiological stress burden (Takeda, H., et al., *Stress Kagaku* 7(1), 90-96, 1992).

[0011] The present inventors have investigated the effect of a cacao bean-derived extract in preventing such stress and in promoting adaptive development. As a result, the present inventors have discovered that a cacao bean-derived extract has superior effects including the prevention of a stress-induced decrease in emotional and behavioral response, and the promotion of adaptive development to counter stress. Details are as described in the preferred embodiments.

[0012] The food or drink item pertaining to the present invention is a food or drink item containing a cacao bean-derived extract, and because said extract is non-toxic to the human body, its added proportion is not specifically limited, but in consideration of individual food or drink characteristics, appealing taste, or economics, the added amount should be approximately from 0.1 to 20% and preferably from 0.2 to 10%. A food or drink item pertaining to the present invention may naturally be one using cacao beans as a primary ingredient, such as chocolate or

cocoa, and provided that it is possible to add the extract pertaining to the present invention, the food or drink item pertaining to the present invention can also be used in various drinks or various food items including cookies, candies, lozenges, jellies, or other sweets; and starch-based foods, chief among them bread and noodles. The extract pertaining to the present invention can also be used in supplementary components customarily used in the food field, for example sugars (including sucrose, liquid sugar, honey, and oligosaccharides), vitamins (including vitamin A and vitamin C), various acids (including citric acid and malic acid), various fragrances, and various tablets, powdered agents, granular agents, and liquid agents. The extract pertaining to the present invention can also be suitably blended in an appropriate stage of manufacturing consistent with various food or drink item characteristics and various objects.

[DESCRIPTION OF THE PREFERRED EMBODIMENTS]

[0013] The present invention is next described in further detail by means of preferred embodiments, but the scope of the present invention is in no way limited to such embodiments alone.

[0014] **FIRST EMBODIMENT** A quantity of 500 wt parts 80% ethanol solution was added to 100 wt parts defatted cacao mass powder, an entire day and night of mixing and extraction was performed at ambient temperature, 10 minutes centrifuge separation at 10,000 rpm was then performed, the supernatant liquid was evaporated under reduced pressure by a rotary evaporator, freeze-drying was performed, and a cacao extract was obtained.

[0015] **SECOND EMBODIMENT** A stress-preventing effect was investigated using the present extract. Using 8-week-old Sprague-Dawley (SD) rats (Nihon Kurea, 7-8 animals per group), experimentation was performed following 1 week of preparatory rearing (with free intake of feed and liquid). The animals were reared in an animal rearing chamber (EBAC-S, Nihon Kurea) under conditions of $23\pm 1^{\circ}\text{C}$ ambient temperature and $55\pm 5\%$ humidity. In the experiment, 0.5% cacao extract obtained in the first embodiment was added to powdered feed (AIN76 refined feed, not added to control group), and free intake was allowed from 10 days prior to the application of stress. A confinement stress was applied for 4 hours by a procedure forcibly confining each animal within a wire cage ($4.5\times 4.5\times 16\text{cm}$). Emotional behavior (changes produced by emotional response) was evaluated by 10 minutes observation using a device capable of simultaneous open field and hole board testing (automatic hole board tester, ST-1, Muromachi, K.K.). Evaluation used the method of Takeda et al. (Takeda, H., et al., Stress Kagaku 7(1), 90-96, 1992), with open field testing indexed by intervals of motion and the number of body raisings, and hole board testing indexed by the number of head dips (hole-peeping). Experimental results are indicated as mean values \pm standard deviation, and Student's t-test was used as a test for significant differences.

[0016] The results as shown in FIG 1 indicate that the amount of motion in the control group declined from $3094\pm 474\text{cm}$ before stress application to $2153\pm 507\text{cm}$ after stress application. In contrast, the cacao extract group displayed no major change, at $3313\pm 296\text{cm}$ and $3296\pm 301\text{cm}$ (significant difference from control group at 5% level of significance).

[0017] As shown in FIG 2, the number of head dips, deemed an emotional behavior, declined from 15.9 ± 6.5 to 10.8 ± 5.4 in the control group, while no change was seen in the cacao extract group, at 16.0 ± 6.9 and 17.6 ± 3.8 (significant difference from control group at 5% level of significance).

[0018] As shown in FIG 3, the number of body raisings declined from 20.4 ± 3.4 to 12.8 ± 4.3 in the control group, while the cacao extract group displayed no major change, at 19.9 ± 5.3 and 19.9 ± 4.8 (significant difference from control group at 5% level of significance).

[0019] **THIRD EMBODIMENT** An effect promoting adaptive development to stress was investigated using the present extract. Using 8-week-old SD rats (Nihon Kurea, 6-8 animals per group), experimentation was performed following 1 week of preparatory rearing (with free intake of feed and liquid). The animals were reared in an animal rearing chamber (EBAC-S, Nihon Kurea) under conditions of $23 \pm 1^\circ\text{C}$ ambient temperature and $55 \pm 5\%$ humidity. A repetitive stress was applied by 7 days repeated performance of a procedure forcibly confining each animal within a wire cage ($4.5 \times 4.5 \times 16\text{cm}$) for a 4 hour interval per day. After 3 days repeated confinement stress was applied, from day 4 onward, 100mg/kg of the cacao extract obtained in the first embodiment was administered orally after application of stress (with the control group given an equivalent quantity of distilled water). Evaluation of emotional behavior was performed as in the second embodiment.

[0020] The results as shown in FIG 4 indicate that after 3 days repeated application of confinement stress of 4 hours per day, body weight in the control group had declined by $0.6 \pm 0.9\text{g}$ compared to the initial value, and that after a further 4 days application of confinement, body weight had declined $6.3 \pm 4.8\text{g}$; thus, a stress response was apparent. In contrast, weight reduction in the cacao extract group was suppressed to $0.4 \pm 2.2\text{g}$ after 3 days, with a weight gain of $0.8 \pm 3.0\text{g}$ after 7 days, indicating promotion of adaptive development (significant difference from control group at 5% level of significance).

[0021] As shown in FIG 5, the interval of motion in the control group declined to $1640 \pm 635\text{cm}$ on day 3 and then to $1455 \pm 372\text{cm}$ on day 7. In contrast, the interval of motion increased in the cacao extract group from $1690 \pm 316\text{cm}$ to $2241 \pm 369\text{cm}$, indicating promotion of adaptive development (significant difference from control group at 5% level of significance).

[0022] As shown in FIG 6, the number of head dips in the control group declined to 14.1 ± 8.1 and then to 9.1 ± 4.6 , while the number of head dips increased in the cacao extract group from 14.1 ± 5.1 to 16.8 ± 5.6 (significant difference from control group at 5% level of significance).

[0023] As shown in FIG 7, the number of body raisings showed no major change in the control group, at 14.3 ± 9.0 and 10.3 ± 5.2 , while the number of body raisings increased in the cacao extract group from 14.1 ± 7.7 to 20.1 ± 9.6 (significant difference from control group at 5% level of significance).

[0024] FIRST PRACTICAL EMBODIMENT

Using the cacao extract obtained in the first preferred embodiment, a cocoa drink with the following composition was prepared according to a common method.

Cacao extract (solid)	0.3	parts
Cacao extract (liquid)	0.35	parts
Cocoa powder	0.5	parts
Granulated sugar	6	parts
Cow milk	6	parts
Almond extract	0.12	parts
Rum	0.1	parts
Stabilizer	0.03	parts
Emulsifier	0.1	parts
Water	86.5	parts

[0025] SECOND PRACTICAL EMBODIMENT

Using the cacao extract obtained in the first preferred embodiment, a jelly drink with the following composition was prepared according to a common method.

Cacao extract (solid)	0.5	parts
Powdered sugar	4	parts
Granulated sugar	10	parts
Fragrance	0.15	parts
Starch syrup	20	parts
Agar	0.35	parts
Water	65	parts

[0026] THIRD PRACTICAL EMBODIMENT

Using the cacao extract obtained in the first preferred embodiment, a lozenge with the following composition was prepared according to a common method.

Cacao extract (solid)	1	parts
Granulated sugar	85	parts
Concentrated fruit juice	5	parts
Citric acid	6	parts
Fragrance	2	parts
Gelatin	1	parts

[0027]

[EFFECT OF THE INVENTION] By including the cacao bean-derived extract pertaining to the present invention in a food or drink item, a stress-induced decrease in emotional and behavioral response can be prevented. Adaptive development, an important defense mechanism of the body against stress, can also be promoted, and an effect of active perception and response to external stress can be anticipated. There is also great significance to the high safety in continued daily usage assured by a long history of use as a foodstuff, as well as the ability for simple and easy procurement at a low cost.

[BRIEF DESCRIPTION OF THE DRAWINGS]

FIG 1 is a graph illustrating the interval of motion before and after application of stress.

FIG 2 is a graph illustrating the number of head dips before and after application of stress.

FIG 3 is a graph illustrating the number of body raisings before and after application of stress.

FIG 4 is a graph illustrating increase or decrease in body weight in a stressed state.

FIG 5 is a graph illustrating fluctuations in the interval of motion in a stressed state.

FIG 6 is a graph illustrating fluctuations in the number of head dips in a stressed state.

FIG 7 is a graph illustrating fluctuations in the number of body raisings in a stressed state.

A1	Figure 1
A2	Fluctuations in interval of motion during application of stress
A3	Interval of motion (cm)
A4	Cacao extract
A5	Before
A6	After

B1	Figure 2
B2	Fluctuations in number of head drops during application of stress
B3	Number
B4	Cacao extract
B5	Before
B6	After

C1	Figure 3
C2	Fluctuations in number of body raisings during application of stress
C3	Number
C4	Cacao extract
C5	Before
C6	After

D1	Figure 4
D2	Fluctuations in body weight from start of application of stress
D3	Grams
D4	Cacao extract
D5	Day 3
D6	Day 7

E1	Figure 5
E2	Fluctuations in interval of motion during application of stress
E3	Interval of motion (cm)
E4	Cacao extract
E5	Day 3
E6	Day 7

F1	Figure 6
F2	Fluctuations in number of head drops during application of stress
F3	Number
F4	Cacao extract
F5	Day 3
F6	Day 7

G1	Figure 7
G2	Fluctuations in number of body raisings during application of stress
G3	Number
G4	Cacao extract
G5	Day 3
G6	Day 7